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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. |
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| 09/295,463 | 04/13/99 | COWSERT L | ISIS-3455 |

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| EXAMINER | |
|---|---|
| MARSCHEL, A | |
| **ART UNIT** | **PAPER NUMBER** |
| 1631 | 10 |

**DATE MAILED:** 01/17/01

***Please find below and/or attached an Office communication concerning this application or proceeding.***

**Commissioner of Patents and Trademarks**

| Offic Action Summary | Application No. 09/295,463 | Applicant(s) Cowsert et al. |
|---|---|---|
| | Examiner Ardin Marschel | Group Art Unit 1631 |

☒ Responsive to communication(s) filed on *Nov 2, 2000*

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

**Disposition of Claim**

☒ Claim(s) *1-54* is/are pending in the applicat

Of the above, claim(s) *1, 2, 5, 21, 22, 25, and 41-46* is/are withdrawn from consideration

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *3, 4, 6-20, 23, 24, 26-40, and 47-54* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☒ Claims *1-54* are subject to restriction or election requirement.

**Application Papers**

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. § 119**

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☒ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____ .

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

**Attachment(s)**

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). *(19 sheets)*

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

***— SEE OFFICE ACTION ON THE FOLLOWING PAGES —***

Applicant's election of Group II (claims 3, 4, 6-20, 23, 24, 26-40, and 47-54) in Paper No. 9, filed 11/2/00, is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (M.P.E.P. § 818.03(a)).

Claims 3, 4, 6-20, 23, 24, 26-40, and 47-54 are rejected, as discussed below, under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 6-20, 23, 24, 26-40, and 47-54 are vague and indefinite because the preambles cite the defining or generating of compounds that modulate expression, are amenable to antisense binding, or for validating the function of a gene or gene product confusingly without any steps that are directed to such modulation of expression, antisense binding, or gene function validation. It is noted that defined criteria are cited but this phrase is so broad that its connection with modulation of expression etc. is completely obscure and unclear. Do applicants intend that any generation of nucleobase sequences be a method within the scope of the claims with some other selection later and undefined in the claims to be imposed for modulation of expression etc? It is noted that generic biological etc.

properties are cited in certain claims but again without any apparent connection with the modulation of expression etc. It is noted that claims 3 and 4 require therein that the virtual compounds modulate target sequence expression according to defined criteria but do not clarify the connection as to these defined criteria which do not seem cited in the claims as to what selection criteria is actually required. Clarification of the metes and bounds of the actual practices of the claims via clearer claim wording is requested.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

Claims 3, 4, 6-20, 23, 24, 26-40, and 47-54 are rejected under 35 U.S.C. § 102(b) as being clearly anticipated by Gilbert (EPO 0,514,927).

In the abstract Gilbert describes an automated sequencer which comprises a oligomer synthesizer, an array, a detector, and

a central computer which defines predicts oligomers. The synthesizer synthesizes them and they are utilized in a detector for sequencing by the property of hybridization. These are the instant methods wherein the computer manipulation of the data and oligomers reads on the above listed instant claims. It is noted that *in silico* is defined in the instant specification on page 7, lines 7-10, as a method wherein it is executed "in a computer manipulatible and reliable form". The computerized devices are also depicted in the reference in Figure 1. On page 3, lines 17-22, these devices work to predict oligomers for each next round of synthesis and detection. The oligomers are predicted based on a target sequence that is being determined during the overall sequencing process or, alternatively, from various starting sequences as summarized on page 17, lines 48-56, which therefore discloses a library of sequences. The prediction of each round of oligomers occurs via a constructed nucleic acid sequence as disclosed in the sentence that bridges pages 3 and 4 of the reference. A more detailed description of these elements and method steps is given on page 5, line 13, through page 17, line 5, with further refinements thereafter. The robotic or automatic computer control of hybridization in the reference is given on page 14, line 4, through page 15, line 55, as also required in the instant claims directed to binding to target nucleic acid sequences. The reduction of oligomers of the virtual design

library for probe selection via a set criteria is given on page 18, lines 6-22, wherein hairpin formation ability removes a potential probe from the set or, alternatively, removal of duplicates is a criteria as also required in the instant claims generically. Hybridization is either a biological, chemical, or physical property that is assayed via the utilization of various membrane bound oligomers in the multiple rounds of sequencing as noted in the reference in the above citations which anticipates instant claims, such as claim 4. Lastly, PCR as a method step in the automated analysis methods of the reference, as required in instant claims 18 etc., for example, is disclosed on page 19, lines 2-4.

Claims 3, 4, 6-17, 19, 20, 23, 24, 26-37, 39, 40, and 47-54 are rejected under 35 U.S.C. § 102(b) and (e) as being clearly anticipated by Hubbell et al.(P/N 5,571,639).

In the abstract of Hubbell et al. a method of formation of arrays wherein a computer system selects probes and designs layouts is summarized. Figure 1 goes further in depicting devices with the method steps of functioning as instantly claimed in that there is a item 100 computer which designs oligomer probes for chip design via utilizing a database which contains target sequences. Beyond this first computer there is a CPU containing synthesizer device and a device for analysis and another for detection. The automated chemical synthesis steps

are deemed to anticipate instant robotic synthesis claims. Array design, synthesis, and assay usage is specifically disclosed in column 3, line 51, through column 5, line 5, which also anticipates the instant claims. Note also that in column 6, lines 1-17, describes target selection from various databases which is well known to inherently contain human sequences, genomic sequences, etc. as required in instant claims 19 and 20, for example. The specific probe design for array preparation is disclosed by the tiling method, for example, in column 6, line 61, through column 9, line 21. Oligomer synthesis is then performed by computer control as given in column 9, line 22, through column 18, line 12. Detection assaying is performed by scanning devices as given in column 18, line 15, through column 19, line 26, as well as discussed hereinabove.

The following is a quotation of 35 U.S.C. § 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
>
> Subject matter developed by another person, which qualifies as prior art only under subsection (f) or (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed

invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103, the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. § 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of potential 35 U.S.C. § 102(f) or (g) prior art under 35 U.S.C. § 103(a).

Claims 3, 4, 6-20, 23, 24, 26-40, and 47-54 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Gilbert (EPO 0,514,927), taken in view of Nickerson et al.(PNAS 87:8923 [1990]).

Gilbert has been summarized above but lacks the usage of automated ELISA assay method steps as required in instant claim 18, for example.

Nickerson et al. describes and motivates the automated ELISA method as described in the MATERIALS AND METHODS section wherein it is performed in an automated robotic workstation for usage in DNA diagnostics as summarized in the abstract and exemplified throughout the reference and specifically depicted in Figure 1 on page 8924.

Thus, it would have been obvious to someone of ordinary skill in the art at the time of the instant invention to perform the methods of Gilbert wherein additionally Nickerson et al. motivates and suggests the practice of robotic DNA diagnostic

ELISA methods as desired thus resulting in the practice of this embodiment of the instant invention.

On the enclosed PTO Forms 1449 three application citations are lined through due to a lack of dates of publication for them as required for citations on such forms. The first two applications have matured into U.S. Patents which have been written in on said forms. The third application, however, seems to be cited in error since there is no Cook et al. application with the U. S. Patent Application serial number 08/762,488.

The disclosure is objected to because of the following informalities:

The disclosure is objected to because it contains an embedded hyperlink and/or other form or browser-executable code. Applicants are required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01. Such code is present in the specification at page 47, line 9.

Correction is required.

No claim is allowed.

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993)(See 37 CFR § 1.6(d)). The CM1 Fax Center number is either (703)308-4242 or (703)305-3014.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ardin Marschel, Ph.D., whose telephone number is (703)308-3894.

The examiner can normally be reached on Monday-Friday from 8 A.M. to 4 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, Ph.D., can be reached on (703)308-4028.

Any inquiry of a general nature or relating to the status of this application should be directed to Patent Analyst, Tina Plunkett, whose telephone number is (703)305-3524 or to the Technical Center receptionist whose telephone number is (703) 308-0196.

January 12, 2001

ARDIN H. MARSCHEL
PRIMARY EXAMINER